

REMARKS

Applicants respectfully request reconsideration of this application in view of the amendments and remarks made herein.

Claims 46-55, 57 and 59-67 are pending in the application. Claims 56 and 58 have been canceled herein without prejudice to the prosecution of their subject matter in any continuing applications. Claims 46, 47, 50-53 59, 60-63 and 66-69 have been amended to more particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully submit that the amended claims are supported by the original disclosure of this application. As such, no new matter has been added by these amendments.

Claim Rejections

1. Claim Objections

Claims 51, 52, 58 and 66-69 were objected to by the Examiner for not reciting SEQ ID NOs 2, 4, 6 and 8 when referring to the various PAP-S proteins. Applicants have amended the claims to specify that the proteins encompassed by the claims are those that either share homology to the protein sequences of SEQ ID NOs 2, 4, 6 and 8 or that are encoded for by nucleic acid molecules that bind under stringent conditions to the nucleic acid sequences of SEQ ID NOs 1, 3, 5, or 7 and capable of inducing cell death. Support for the amendments to the claims can be found in paragraphs [0029]-[0030] of the specification. Applicants respectfully request that the objections to claims 51, 52, 58 and 66-69 be withdrawn by the Examiner.

2. The Claims Are Definite

The Examiner rejected claims 68-69 under §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Examiner, the claims are indefinite because the PAP-S α protein and the PAP-S β protein lack antecedent basis in claim 46. Applicants have amended claims 68 and 69 to correct the antecedent basis. Applicants respectfully request that the rejections to claims 68-69, under §112 second paragraph, be withdrawn by the Examiner.

3. The Claims are Enabled to Person of Skill in the Art to Practice the Invention

Claims 46-65 were rejected by the Examiner under 35 U.S.C §112, first paragraph. The Examiner alleges that although the specification, while being enabling for a method of inducing nematode resistance in a transgenic plant by introduction of a chimeric gene comprising the pokeweed antiviral protein (PAP) encoding sequences under the control of a nematode inducible promoter in a transgenic plant, does not reasonably provide enablement for a method of inducing cell death in any plant cells with the exemplified or non-exemplified pokeweed encoding nucleic acids. The Examiner further maintains that the prior art teaches that transformation of a plant with a PAP encoding nucleic acid is highly unpredictable. The Examiner alleges that Applicants' own working example demonstrates the unpredictability inherent in transforming a plant with any nucleic acid encoding PAP because transformation of tobacco cells with mature PAP-S encoding sequences under the control of a inducible promoter failed to produce transformed tobacco cells.

Applicants disagree with the Examiner's characterization that transformation with PAP encoding nucleic acids "highly unpredictable." In order to advance prosecution of subject matter that the Examiner believes would qualify to be not highly unpredictable, Applicants have amended claim 46 to recite that the nucleic acid molecule encoding pokeweed antiviral protein is "a pro-PAP-S protein, PAP-S β protein, or PAP-S α protein." Applicants respectfully invite the Examiner's attention to the working examples of the specification which clearly demonstrate that transformation of pro-PAP-S, PAP-S β , or PAP-S α GUS constructs into tobacco protoplasts resulted in inhibition of ribosome activity.

Furthermore, claims 47 and 63 have been amended to refer specifically to potato plants, which addresses the Examiner's concerns about tobacco plants engineered to express mature PAP-S. Accordingly, Applicants respectfully submit that these and all pending claims satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. Applicants respectfully request that this ground of rejection be withdrawn.

4. Claims are Not Obvious in View of the Cited Art

A. The Examiner has rejected claims 46, 50, 54-55, 57 and 59-62 under 35 U.S.C. § 103(b) as being unpatentable over Tumer (WO99/60843) in view of Thomas (US6, 140, 554).

According to the Examiner, Tumer teaches a method of producing transgenic plants expressing a chimeric gene comprising a nucleic acid encoding pokeweed antiviral protein designated PAP-II, including full length, wild type, and a truncated protein PAP II with

deleted C-terminal, operably linked to a promoter expressible in plant cells; said promoter can be a pathogen inducible or tissue-specific for expression of said promoter in tissue-special manner or inducible by a pathogen. Further, the Examiner maintains that Thomas teaches methods of producing nematode resistant transgenic plants using cell-specific promoters such as KNT1 and RB7. According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of transforming a plant with a pokeweed antiviral protein encoding DNA to induce viral or fungal resistance as taught by Tumer and to modify that method by incorporating any of the inducible promoters known in the prior art such as KNT1 or RB7 as taught by Thomas.

Tumer teaches expression of a different pokeweed antiviral protein, PAP-II, not PAP-S protein. Furthermore, although Tumer teaches that transgenic plants expressing PAP-II exhibit both antiviral and antifungal activity, such expression results in little to no plant cell death (see, p.3, lines 16-23 of Tumer). For example, Tumer discloses the expression of PAP II in turf grass and states that such “transgenic plants were indistinguishable from wild type plants in their physical characteristics and appearance, indicating that PAP II expression was not toxic to turfgrass” (see, p. 31, lines 28-30 of Tumer). Since the claims of the present invention are directed to induction of cell death through the expression of PAP-S proteins, it can be said that, if anything, Tumer teaches away from the present invention. Furthermore, Thomas, fails to correct the deficiencies in Tumer, as Thomas does not teach the use of PAP, much less a PAP precursor, pro PAP-S, PAP-S α or PAP-S β .

Taken alone, or in combination, Tumer and Thomas do not disclose, teach or suggest the claim invention. Applicants assert that claims 46, 50, 54-55, 57 and 59-62 are not rendered obvious in view of the references. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

B. The Examiner has rejected claims 46-65 under 35 U.S.C. § 103(b) as being unpatentable over Tumer (WO99/60843) and Kanieswski (US 6,015,940) in view of Thomas (US 6, 140, 554) and Poyet (FEBS 409:97-100).

According to the Examiner, Tumer teaches a method of producing transgenic plants expressing a chimeric gene a nucleic acid encoding pokeweed antiviral protein designated PAP-II, including full length, wild type, and a truncated protein PAP II with deleted C-terminal, operably linked to a promoter expressible in plant cells; said promoter can be a pathogen inducible or tissue-specific for expression of said promoter in tissue-special manner or inducible by a pathogen. According to the Examiner, Kanieswski teaches a method of

inducing viral resistance in tobacco and potato plants and plant cells, the method comprising transforming said plants and plant cells with a chimeric gene comprising a DNA sequence encoding PAP' or a mutant retaining PAP activity, a tissue specific or inducible promoter, N-terminal signal sequence capable of targeting said PAP' in specific cells of the plant. Further, the Examiner maintains that Thomas teaches methods of producing nematode resistant transgenic plants using cell-specific promoters such as KNT1 and RB7. Finally, according to the Examiner, Poyet teaches the isolation and characterization of nucleic acids encoding SEQ ID NO:2, 4, 6, 8 or nucleic acids that hybridize to SEQ ID NO; 1,3, 5 or 7 and encoding proteins with PAP-S activity.

The Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of transforming a plant with a pokeweed antiviral protein encoding DNA to induce viral or fungal resistance as taught by Tumer and to modify that method by incorporating any of the inducible promoters known in the prior art such as KNY1 or RB7 taught by Thomas, without unexpected results. The Examiner maintains that one would have been motivated to use any of the PAPs known in the prior art as taught by either Tumer, Kanieswski or Poyet, with any known promoter, given the antiviral, antifungal disease resistance activity in transgenic plants as taught by each of Tumer, Kanieswski or Poyet and nematode resistance activity as suggested by Tumer.

Applicants assert that neither Tumer, Kanieswski nor Thomas disclose, teach or suggest, alone or in combination, the use of PAP-S, much less the use of pro-PAP-S, PAP-S α or PAP-S β to induce cell death in transgenic plants. Poyet merely teaches the cloning and expression of PAP-S in *E. coli*. As indicated above, although Tumer teaches that transgenic plants expressing PAP-II exhibit both antiviral and antifungal activity, such expression results in little to no plant cell death (see, p.3, lines 16-23 of Tumer). In fact, Tumer teaches away from the present invention. None of the additionally cited references of the Examiner cure the deficiency of the teaching of Tumer.

It should also be noted that, for the claims 46, 48, 49, 59 and 64-69, the prior art fails to disclose that such PAP-S α or PAP-S β would work independently of one another. As indicated in [0021] of the specification, "on the basis of structural predictions, PAP-S α contains the RNA recognition motif and ribosome binding domain regions, whilst PAP-S β contains the critical catalytic residue site." Surprisingly, expression of either the PAP-S α or PAP-S β protein alone results in a significant inhibition of ribosome activity.

Furthermore, Tumer and Kanieswski teach the use of constitutive promoters and not the use of inducible promoters. Although, Thomas teaches the use of nematode resistance

promoters, there is no motivation to combine this document with the teachings of Tumer, Kanieswki or Poyet to arrive at Applicants' invention. Applicants maintain that without the use of hindsight a skilled person would have no reason to use a precursor PAP-S, pro PAP-S, PAP-S α or PAP-S β under the control of a inducible promoter for inducing cell death in a plant. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

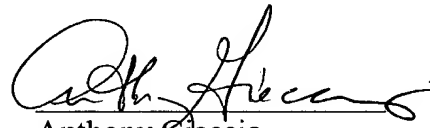
CONCLUSION

Applicants respectfully submit that all pending claims of this application are presently in condition for allowance. Prompt and favorable reconsideration and allowance of all pending claims is respectfully requested.

The Commissioner is authorized to charge any fees relevant to this filing to Deposit Account No. 11-0600. The Examiner is invited to contact the undersigned to discuss any matter in this application.

Respectfully submitted,
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